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(54) Title: INHIBITION OF FATTY ACID SYNTHASE AS A MEANS TO REDUCE ADIPOCYTE MASS

## (57) Abstract

Weight loss was noted in nude mice treated with cerulenin, a non-competitive inhibitor of FAS. Sustained reduction of adipocyte mass in humans without toxicity would significantly impact disease prevention worldwide. Aside from psychological and self-esteem improvement, weight loss via reduction of adipocyte mass may: (1) ameliorate hyperglycemia associated with non-insulin-dependent diabetes mellitus thereby reducing diabetic complications such as arterial disease, blindness, cataracts, etc., (2) reduce hypertension, (3) reduce risk of coronary artery vascular disease and stroke, and (4) reduce the risk of other complications of massive obesity such as osteoarthritis, surgical complications, etc. There is also potential use in livestock and poultry to reduce the saturated fat content of meat products. Therefore FAS inhibitors are disclosed herein as novel agents for weight reduction. A family of compounds ( $\gamma$ -substituted- $\alpha$ -methylene- $\beta$ -carboxy- $\gamma$ -butyrolactones) whose synthesis was based on the cerulenin motif is shown herein to inhibit fatty acid synthesis, inhibit growth in certain susceptible tumor cells, and induce weight loss.

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